REMARKS

Claims 29 and 30 are pending in the present application. All other claims were canceled by preliminary amendment on October 20, 2003. By virtue of this response, claims 29 and 30 and the specification have been amended to clarify applicant's meaning. Accordingly, claims 29 and 30 are currently under consideration. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented. Support for the amendments may be found in the specification as filed, including in the claims as filed. It is believed that no new matter was added by virtue of these amendments to the specification and the claims.

Request for Amended Specification

The examiner objected to the specification as allegedly "not in the proper English vernacular." In response, applicant reviewed the specification and submits herewith amendments to correct various grammatical errors and to add SEQ ID NOs.

Rejections under 35 USC § 112

Claims 29 and 30 stand rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner stated that claim 29 was unclear, and suggested suggested replacing the term "functional" with "sensitive." Applicants have amended claim 29 as the examiner suggested.

The Examiner stated that claim 30 was indefinite because it was allegedly "unclear if the target sequence is recognized by the P transposase, or if it is mutated in such a manner that it is no longer recognized by the P transposase ... [as well as] for the recitation of the phrase '(e) missing of DNA sequences other than those defined in item (1) or item (2).'"

Applicants do not agree that it is unclear whether or not the target sequence is recognized by the P transposase. With regard to the relationship between the target sequence and the P-transposase, generally a transposition is induced after the P-transposase binds to the target sequence, in other words, the target sequence is identified by the P-transposase so as to activate the transposition. If the target sequence is mutated to an incomplete target sequence by losing a portion of sequence thereof, or another intervening sequence, the P-transposase is unable to bind the target sequence and the transposition is not induced. Further, claim 29, from which claim 30 depends, recites that the *Drosophila* clipped FRT (cFRT) chromosome is insensitive to a P transposase. However, to expedite prosecution, claim 30 was amended to recite that the chromosome "is generated through damage and alteration of a target sequence to an incomplete target sequence."

With regard to the recitation of the phrase "(3) missing of DNA sequences other than those defined in item (1) and in item (2)", applicant has deleted this recitation in the pending claims.

The Examiner also suggested amendment to claim 8. Applicant thanks the Examiner for commenting on claim 8. However, per the preliminary amendment filed on the same day as this application was filed, claim 8 is not pending in this application. Therefore applicants believe such an amendment is not required at this time.

Rejections under 35 USC § 101

Claim 29 stands rejected under 35 USC § 101 because the claimed invention as allegedly directed to non-statutory subject matter. The Examiner alleged that "[a]ny mutation of the P5' or P3' region *could* prevent transposition, therefore, causing the chromosome to be insensitive to the *P*-transposase, but sensitive to a yeast FLP." Emphasis added. The Examiner further alleged that there is no indication of the hand of man is involved. The Applicant disagrees with the Examiner's characterization.

Firstly, the FLP-FRT system has become more frequently used in mouse research, and involves the use of flippase (FLP) recombinase, derived from *Saccharomyces cerevisiae* (yeast). The FLP/FRT recombination system belongs to a kind of site-specific recombination whose unique

characteristic resides in its specificity. FLP recognizes a pair of FLP recombinase target (FRT) sequences flanking the genomic region of interest. The mentioned recombination is often induced between two respective same sequences in short length (less than 50 base pairs), and more importantly, the frequency of such recombination is quite high over other recombination systems. FLP is a site-specific recombination and FRT is the corresponding sequence identified by FLP. **Until now, FRT sequence has still not found in several kinds of animal models, such as mouse, *Nematoda* and *Drosophila*. Therefore, applicant submits that the Examiner's has not shown that there is no indication that the hand of man is involved in generating a Drosophila clipped FRT chromosome.**

Incorporating FRT sequence into the second chromosome of Drosophila could be done by artificial manipulations. Since there exists no FRT or related sequence in the chromosome of *Drosophila*, a recombination could be induced by treating the clipped FRT thereinto with the FLP solution.

Secondly, the clipped FRT sequence is manipulated into P-transposon of the second chromosome of Drosophila, which is called P[FRT] insertion. According to the description for P-transposase treatment in paragraphs [0058] - [0066] of the present specification, the cFRT2L and the cFRT2R are insensitive to P transposase and can not be mobilized by P transposase. Furthermore, several selection markers may be selected to be incorporated into cFRT insertion, such as the X-linked germline-dependent dominant female sterile mutation, ovoD1, mini-white+ gene and rosy+ gene, so that once any mutation is generated, the subsequent procedure to identify the mutated point will be facilitated by these selection in the FLP-FRT system.

As above, the technical feature of the present invention lies in the clipped FRT sequence with an optional artificial selected marker and thus any mutation of nucleic acids could be quickly found out by inverse PCR (IPCR) or plasmid rescue methods. Establishing such cloning model system will extensively promote the development for treating human disease by solving the genomic projects of different species more quickly. Therefore, the living subject of the present invention is indeed achieved by artificial intervention and creates a tremendously useful

improvement in the existing cloning system, so that the subject matter of the present invention complies with the stipulations of 35 USC §101 and the regulations of MPEP 2105.

As a further matter, the present application is divided from U.S. Patent No. 6,962,804, which claimed a method for generating a Drosophila clipped FRT (cFRT) chromosome insensitive to a P transposase but remaining functional to a yeast site-specific flippase recombinase (FLP). Therefore, it seems to the applicant that the product, a *Drosophila* clipped FRT (cFRT) chromosome, made from the method should also be patenable.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. **529872000111**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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